SQUAMOUS CELL CARCINOMA OF THE BLADDER IN A 25-YEAR-OLD MALE COMPLICATING A CASE OF VESICAL AND EXTRA-VESICAL SCHISTOSOMIASIS: A CASE REPORT AND LITERATURE REVIEW

ABSTRACT

Background: Schistosomiasis, a neglected tropical disease caused by parasitic flatworms, rarely presents with squamous cell carcinoma (SCC) of the bladder. We report a unique case of SCC of the bladder in a young male with concomitant schistosomiasis and extensive extra-vesical involvement.

Case Presentation:

A 25-year-old male presented with gross hematuria and lower abdominal pain.

Diagnostic workup including complete blood count, renal function test, bilateral upper extremities, creatinine, Abdominopelvic Ultrasound, Computer Tomography scan was done. A diagnostic Cystoscopy with biopsy revealed a huge Bladder mass and confirmed as SCC of the Bladder on biopsy.

Intraoperatively, a huge bladder mass was found, the Appendix and omentum were adhered to the Urinary bladder.

A palliative radical cystectomy with Urinary diversion using ileum conduit was carried out. Appendectomy and partial Omentectomy were also carried out.

Histopathological examination of resected tissues confirmed schistosomiasis-induced pathology, SCC of the Bladder with schistosoma eggs infiltrating the appendix and omentum, indicating disseminated disease.

Conclusion: This case underscores the rare co-occurrence of SCC of the bladder and disseminated schistosomiasis in a young adult. Timely identification of schistosomiasis and

suitable antiparasitic treatment, together with consistent monitoring for possible sequelae, is essential in mitigating the risk of SCC. Heightened awareness among healthcare workers, particularly in endemic regions, is essential for the early identification and timely management of schistosomiasis. Moreover, public health initiatives focused on managing schistosomiasis via enhanced sanitation, health education, and mass medicine distribution are essential for reducing the incidence of schistosomiasis-related cancers.The results of this case indicate a necessity for additional investigation into the pathophysiological pathways connecting schistosomiasis to bladder cancer, especially in younger demographics, and for the formulation of targeted screening methods for at-risk persons.

Keywords: ***squamous cell carcinoma, bladder cancer, schistosomiasis, parasitic infections, Radical Cystectomy, ileum conduit.***

INTRODUCTION

Schistosomiasis is a water borne parasitic infection and after malaria, the most common tropical diseases in the world. It is endemic in 5 developing countries and 2 million people, most of them in rural and suburban areas, have this parasitic infection[1]. Bladder cancer (BC), a multifaceted disease encompassing various histopathological types, poses a significant global health burden. Histological Variants include Urothelial cell carcinoma, Squamous cell carcinoma, Adenocarcinoma, small cell carcinoma of the Bladder, Lymphoma, and Sarcomas [2].Bladder cancer is the 7th most commonly diagnosed cancer in the male population worldwide, whilst it drops to the 10th position when both genders are considered[3]. The worldwide age-standardised incidence rate per 100,000 person/year is 9.5 in men and 2.4 in women [3].

Its etiologyspans a spectrum of risk factors, from cigarette use to occupational exposures, but one intriguing subset is squamous cell carcinoma (SCC), particularly prevalent in regions endemic to Schistosoma haematobium infection [4]. Other risk factors for bladder cancer include environmental exposure such as chlorinated drinks, and exposure to arsenic in drinks [4].

Squamous cell carcinoma of the bladder is an uncommon and severe kind of bladder cancer, representing around 3-5% of all bladder cancer cases in industrialised nations. It is typically linked to persistent inflammation and irritation of the bladder mucosa. Schistosoma

haematobium infection, a parasite disease impacting the urinary system, is a significant risk factor for SCC in specific endemic locales[5].Chronic infection with Schistosoma can result in bladder inflammation, fibrosis, and metaplasia, which may subsequently progress to squamous cell carcinoma over time. Nonetheless, in non-endemic areas and among young persons, squamous cell carcinoma of the bladder attributable to schistosomiasis is exceptionally uncommon[65].

Schistosomiasis, caused by parasitic trematodes, affects millions worldwide, predominantly in sub-Saharan Africa, the Middle East, and parts of South America[7]. Chronic infection with Schistosoma haematobium not only leads to debilitating urogenital symptoms but also predisposes individuals to the development of SCC of the bladder through its inflammatory and potentially carcinogenic effects on urothelial tissues[8].

This review aims to explore the intricate relationship between schistosomiasis and SCC of the bladder, focusing on epidemiological patterns, underlying pathophysiological mechanisms, clinical manifestations, and current management strategies. By shedding light on this unique association, we hope to underscore the importance of targeted interventions and public health initiatives aimed at prevention, early detection, and effective treatment in endemic areas.

CASE PRESENTATION

A 25-year-old male was referred from a district Hospital to the Urology Department on account of recurrent gross Hematuria and Anemia as well as an Ultrasound report suggestive of Bladder Tumor. He is a farmer and has also worked in a mining area in the past.The Patient has been having intermittent gross Hematuria for about a year associated with irritative Urinary symptoms and a feeling of lower abdomen mass and pain. He had several blood Transfusions prior to the referral.

He had symptoms and signs of anemia with dizziness and easy fatiguability. There was significant weight loss.

Abdominal Exam: A huge mass was visible in the suprapubic region, mildly tender on palpation, was moderately mobile,

He was conscious and alert, Chest findings were normal.

An initial full blood count revealed a Hemoglobin of 7 g/dl, moderately elevated WBC and normal Platelet count. The renal function test was mildly impaired with a creatinine of 145umol/L. The Patient was transfused with 3 Units of blood to raise the Hemoglobin to 11 g/dl. The Clotting Profile was normal, ECG was also ok.

Clinical Exam Findings: Young male Adult, looks chronically ill, pale, Cachetic, Afebrile, anicteric, Hydration was fair. His eastern cooperative oncology group (ECOG) performance status was 0.

Imaging and Ultrasound: The Bladder is distended grossly with evidence of a thickened wall and debris noted within it. There is a hypoechoic lesion measuring about 10x7x8 cm with a volume of about 400 cc within the bladder. Bilateral Hydroureteronephrosis.

Diagnostic Cystoscopy showed a Necrotizing bladder tumour, occupying the anterior and right lateral walls of the bladder and protruding towards the base, the mass bleeds easily on contact, with irregular surface. Bimanual palpation revealed mobile rectal mucosa.

Staging/metastatic workup; CECT Scan of Abdomen and Thorax Report;

Urinary Bladder mass with Luminal Narrowing and resultant bilateral Hydroureteronephrosis, Urinary bladder and bilateral Ureteric Calcification.

No evidence of regional Lymphadenopathy, the major vessels are normal.

Both Lungs are free with no signs of lung metastasis.

Surgical Management: Based on the histology and clinical findings and due to the young age of the Patient, extensive counselling was done on the Prognosis, and informed consent was sought for palliative Resection.

An anaesthetic assessment was done, Patient was optimised by transfusing 3 units of whole blood. The haemoglobin before Surgery was 11 g/dl.

Using a lower Midline incision a radical Cystectomy was carried out. Intraoperatively the tumour was fixed on the left pelvic wall, and the appendix and Part of the Omentum were attached to the Bladder.

A palliative Cystectomy was done with Urinary diversion using Ileum Conduit, appendectomy, and partial Omentectomy were also carried out.

The histology revealed a squamous cell carcinoma infiltrating the bladder wall as large anastomosing masses and islands of pleomorphic moderately differentiated squamous cells with no keratin production. The tumour has traversed the full thickness of the bladder and serosal. Intermixed with the tumour masses are numerous viable and calcified Schistosoma ova. Deposites of the tumour and the ova are seen in the omentum. While the ova alone are seen within the lumen of the appendix.

Postoperatively, the Patient recovered uneventfully, and the wound healed without Problems. 6 weeks post-surgery the Patient was seen and reviewed at the clinic doing well and was subsequently referred to the Oncology Unit for assessment and possible initiation of palliative Chemotherapy.

DISCUSSION

Schistosomiasis of the bladder is caused by parasitic Schistosoma species, particularly Schistosoma haematobium Schistosomiasis is an endemic disease in regions of the tropics such as Africa, primarily affecting poor rural people who lack access to safe drinking water and proper sanitation. Activities that expose humans to contaminated natural freshwater sources, such as fishing, agriculture, washing clothing, or swimming, cause infection.In these regions, schistosomiasis accounts for a significant proportion of bladder cancer cases, particularly in young adults, contrasting with the typical age distribution of bladder cancer in non-endemic areas[3]. Our patient is a peasant farmer who is exposed to all these risk factors. Schistosoma is a well-established risk factor for squamous cell carcinoma of the bladder usually occurring in a younger age group and at an advanced stage due to late presentation because of non-specific symptoms. Regarding our patient, he is young, 25-years-old, and presented in the advanced stage with metastasis to the appendix, and omentum.

Even though the exact mechanism underlining the pathogenesis of bladder cancers associated with schistosomiasis, Its causative role is largely admitted and frequently proven by epidemiological [8] studies that usually show associated parasite eggs within the tumour as seen in

the histology of this patient sample. The persistent infection leads to persistent irritation and inflammation with subsequent urothelial damage, predisposing to squamous metaplasia and subsequent malignant transformation[8].

Schistosoma eggs induce a granulomatous reaction, perpetuating the inflammatory cascade and promoting genomic instability conducive to carcinogenesis [9–11]. Typical case presents with lower Urinary tract symptoms and intermittent painless haematuria which were all present in our patient.

Diagnostic workup includes blood workup to rule out Anemia and function of other systems. In our patient, there was moderate anaemia and mildly deranged kidney function. Imaging modalities include Ultrasound of Abdomen and pelvis.

A diagnostic Cystoscopy with biopsy or a TUR BT gives tissue for histological confirmation.

Staging examination involves Contrast-enhanced CT of the abdomen and thorax. In early disease radical or partial Cystectomy is curative, but in locally advanced diseases like in our case, multimodal therapies including adjuvant chemotherapy, radiotherapy or palliative chemotherapy are all employed.The management of advanced bladder SCC secondary to schistosomiasis typically involves radical cystectomy with extended resection to address metastases, followed by adjuvant chemotherapy. Surgical intervention aims for complete resection of the primary tumor and metastatic lesions to improve long-term outcomes. Adjuvant chemotherapy regimens, commonly utilizing cisplatin-based combinations, aim to eradicate residual disease and reduce the risk of recurrence[12].

Literature supports the efficacy of radical surgery in achieving disease control and improving survival in cases of advanced bladder SCC[13,14]. However, the optimal chemotherapy regimen and duration remain areas of ongoing research and clinical investigation.Laboratory findings, including the detection of parasitic eggs in urine, white granulomas, and nodular thickening of the bladder wall during the acute phase, as well as fibrotic lesions linked to severe inflammation, ureteric dilatation, and curvilinear calcifications with numerous calcified dead eggs, are observed along the bladder wall in the chronic phase. These findings can be identified through cystoscopy, urography, or contrast-enhanced computed tomography to aid in diagnosing the disease. Currently, medicinal and surgical interventions are recommended based on the patient's

condition. Praziquantel, the preferred medication for adult worms, effectively heals 80–90% of patients, resulting in a 90% decrease in egg secretion. Damage to the bladder, urethra, and renal parenchyma tissue remains unrepaired, and the patient has examination every six months to avert symptom recurrence and ensure complete elimination of parasite eggs[15].

Prognosis in advanced bladder SCC secondary to schistosomiasis remains challenging, primarily due to the high propensity for local recurrence and distant metastases. Factors influencing prognosis include tumour stage, presence of metastases, histological grade, and response to treatment. Despite aggressive therapeutic approaches, long-term survival rates are generally poorer compared to other bladder cancer subtypes, underscoring the aggressive nature of SCC arising from chronic schistosomiasis[16,17]. Pathological investigations elucidate the sequence from chronic inflammation to squamous metaplasia and eventual malignancy, providing insights into potential targets for therapeutic intervention [18,19].

Treatment strategies emphasize the importance of early detection and aggressive management. Radical cystectomy remains the cornerstone of treatment for localized disease, while adjuvant chemotherapy aims to improve outcomes in advanced stages. Recent advancements in immunotherapy and targeted therapy hold promise for future treatment paradigms, aiming to enhance survival outcomes and reduce treatment-related morbidity [20,21].

Complications of Bladder cancer

Untreated or Advanced bladder cancer will eventually spread to distant organs such as lymph nodes, liver, lungs and bone spread which may eventually lead to death of the patient. Locally advanced bladder cancer will cause hydronephrosis as in our patient which will eventually lead to renal failure requiring dialysis or death of the patient. Bladder pain and recurrent bleeding from the cancer will also lead to Anemia requiring repeated blood transfusions.

CONCLUSION

Squamous cell carcinoma of the bladder is an uncommon variant of bladder cancer, particularly in younger populations, and its correlation with schistosomiasis underscores the importance of endemic diseases in carcinogenesis. A 25-year-old man comes with bladder squamous cell

carcinoma, worsened by schistosomiasis, a parasite illness caused by Schistosoma haematobium, which is known to produce persistent inflammation, fibrosis, and malignant transformation of the bladder epithelium.This case is characterised by the dissemination of Schistosoma eggs from the bladder to the appendix and omentum, indicating an aggressive variant of the illness with extensive infiltration. This underscores the significance of early identification and treatments in schistosomiasis-endemic regions to avert long-term consequences such as cancer. Although SCC is uncommon in young individuals, this case highlights the need of examining parasite infections as potential contributors to cancer in areas where schistosomiasis is endemic.The prognosis of bladder squamous cell carcinoma linked to schistosomiasis is unfavourable due to delayed diagnosis, the malignancy's aggressive characteristics, and the common invasion of surrounding tissues. A comprehensive strategy incorporating surgery, chemotherapy, and even radiotherapy, in conjunction with antiparasitic medication, is essential for effective management. Public health interventions targeting schistosomiasis in endemic regions are crucial to avert future consequences.Chromic Schistosoma haematobium infection is a significant public health issue in endemic regions due to persistent irritation, tissue damage and inflammation caused by its ova. There is an epidemiological link between schistosomiasis and bladder cancers, which are usually squamous cell carcinomas which present at a young age in the advanced stage. These cancers are aggressive with poor prognosis, so therefore, eradication of the Schistosoma parasite by addressing the risk factors for transmission, remains the surest way of preventing this life-threatening disease.

Clinical message:

This case report highlights the occurrence of Bladder cancer in a very young Patient and the complications that can result from late Presentation. Clinicians should be aware of the relationship between schistosomiasis and chronic bladder Inflammation that can result in squamous cell cancer of the bladder.

Clinicians are by this case encouraged to pay attention to especially young Patients presenting with irritative Urinary Symptoms and recurrent haematuria. Appropriate investigations should be initiated to rule out bladder tumours.

Patient Consent:

The authors certify that they have obtained all appropriate patient consent forms.

The patient has permitted his images and other clinical information to be reported in the journal.

The patient understands that his name and initials will not be published and due efforts will be made to conceal his identity, but anonymity cannot be guaranteed.

Ethical Approval: Ethical approval was obtained for the publication of this case report.

Conflicts of Interest: There is no conflict of interest.

Ethical approval: Based on our institutional policy, ethical approval is not required for case reports.

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